REMARKS

These remarks are in response to the Office Action mailed September 13, 2004. Claim 1 has been amended and Claim 2 has been canceled without prejudice to Applicant's right to prosecute the canceled subject matter in any divisional, continuation, continuation-in-part or other applications. No new matter has been introduced.

REJECTION UNDER 35 U.S.C. §103

The Final Office Action indicated that claims 1-5 and 7-10 stand rejected under 35 U.S.C. §103 as allegedly unpatentable over Hall et al. (WO98/44938 ("Hall 1")) or Hall et al. (Human Gene Therapy 11:983-993, 2000) ("Hall 2") or Liu et al. (J. of Virology 74:5320-5328, 2000) or Gordon et al. (Cancer Research 60:3343-3347, 2000) in view of Kurane et al. (Annals of Surgery 4:579-585, 1997) and Borrello et al. (Human Gene Therapy 10:1983-1991, 1999). Applicants respectfully submit that claims 4-5 and 7-8 are not pending in the application. Applicants respectfully traverse this rejection.

Applicants respectfully remind the Examiner that a *prima facie* case of obviousness requires some reasonable expectation of success when the cited references are combined. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); MPEP §2143.02. Whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Int'f. 1986); MPEP §2143.02.

The Examiner indicated in the Office Action mailed August 21, 2003, at page 3, that the field of gene transfer *in vivo*

continues to be *unpredictable and inefficient* (emphasis ours). Thus, there can be no reasonable expectation of success based upon a combination of references that do not teach each and every element of the invention. Combining the references in any order does not generate a predictable and efficient method. Furthermore, Applicants submit that the combination of the references do not teach each and every element of Applicants' claimed invention.

Applicants respectfully submit that the disclosure provided by "Hall 1" is not enabling for treating cancers using a retroviral particle comprising a modified viral surface protein comprising a von Willebrand collagen binding domain and a polynucleotide encoding GM-CSF. For example, the Examiner is directed to pages 21-22 of "Hall 1", which describes methods of treating tumors. In the description there is no reference of GM-CSF expression to treat such tumors. In addition, "Hall 1" fails to demonstrate the treatment of tumors *in vivo*. Accordingly, Hall 1 is not enabled nor does it provide a reasonable expectation of success in treating tumors *in vivo*. Furthermore, the Examiner admitted in the prior office action that "Hall 2", Liu et al. and Gordon et al. do not teach a targeted vector comprising a cytokine or GM-CSF (see page 6 of the prior office action). Thus the primary references (Hall 1, Hall 2, Liu et al. and Gordon et al.) fail to teach and every element of Applicant's claimed invention.

In order to overcome that deficiencies of "Hall 1", "Hall 2", Liu et al. and Gordon et al., the Examiner combines Kurane et al., and Borrello et al. for the teaching that cytokines can be used as adjuvants. The secondary reference fail to teach or suggest how to use cytokine in gene therapy.

Furthermore, in keeping with the Patent Office's position on gene therapy and gene delivery (as stated in the prior office

action mailed August 2, 2003), Applicants submit that to arrive at Applicants' invention by combining the teachings as alleged by the Patent Office would require undue experimentation because gene delivery/therapy is admittedly highly unpredictable by the Patent Office. Thus, there would be no reasonable expectation of success in combining the teachings of the references.

Applicants demonstrate herein that expression of GM-CSF at tumor locations resulted in reduced tumor mass. In addition, Applicants demonstrate the unexpected result of GM-CSF expression including recruitment of host mononuclear cells to the cite of the tumor thereby promoting tumor degradation. Such unexpected results are not taught or suggested by the cited references either alone or in combination. Furthermore, the references either alone or in combination do not teach or suggest how to design or express Applicants' claimed vector.

Applicants submit a *prima facie* case of obviousness requires a reasonable expectation of success. In light of the teachings of the references and the position of the Patent Office, one of ordinary skill in the art would not have any reasonable expectation of success in combining mere cytokine therapy with gene delivery. Nothing in the art cited by the Examiner indicates success of Applicants' claimed invention or a probability of success, thus it would not have been reasonable to expect the success of the instant invention until it was reduced to practice.

Applicants submit that there is no enabling disclosure that provides methods to construct a vector as claimed by Applicants. Furthermore, there is no enabling disclosure that provides evidence that such gene delivery using a vector of the invention can be used to treat tumors. Thus, Applicants have provided a showing there was no reasonable expectation of success thus supporting the position that the claimed invention is

nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA1976); MPEP §2143.02. See also *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991).

For at least the foregoing reasons, Applicants respectfully request withdrawal of the §103 rejection over the cited references.

Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 10/13/04

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